Sensory feedback signal derivation from afferent neurons

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I Summary of the Overall Project

In this study we are exploring the feasibility of extracting 1) cutaneous sensory information about fingertip contact and slip, and 2) proprioceptive sensory information about wrist or finger position. We use implanted nerve cuff electrodes to record peripheral nerve activity in animal models.

Our overall **objectives** for the 3-year duration of this contract are as follows:

1. Investigate, in cadaver material, implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded.
2. Select a suitable animal preparation in which human nerve dimensions and electrode placement sites can be modeled and tested, with eventual human prosthetic applications in mind.
3. Fabricate nerve cuff electrodes suitable for these purposes, and subcontract the fabrication of nerve cuff electrodes of an alternate design.
4. Investigate the extraction of information about contact and slip from chronically recorded nerve activity using these animal models and electrodes. Specifically,
   a. Devise recording, processing and detection methods to detect contact and slip from recorded neural activity in a restrained animal;
   b. Modify these methods as needed to function in an unrestrained animal and in the presence of functional electrical stimulation (FES);
   c. Record activity for at least 6 months and track changes in neural responses over this time.
5. Supply material for histopathological examination from cuffed nerves and contralateral controls, from chronically implanted animals.
6. Investigate the possibility of extracting information about muscle force and limb position from chronically recorded neural activity.
7. Cooperate with other investigators of the Neural Prosthesis Program by collaboration and sharing of experimental findings.

II. Summary of our Progress in Previous Quarters

In the first quarter we completed objective 1 and made progress toward objectives 2 and 3. In three human cadaver arms, we found appropriate implantation sites for nerve cuff electrodes from which cutaneous and proprioceptive information relevant to the human fingers, hand and forearm could be recorded. We selected the cat forelimb as the animal preparation in which human nerve dimensions and electrode placement sites are being modeled and tested. We investigated the details of the innervation of the paw and the forelimb musculature in three cats, identified several possible implantation sites, and started to design cuff electrodes suitable for these purposes.

In the second quarter we built 38 nerve cuff electrodes in assorted sizes, suitable for implantation on four nerves in the left forelimb of cats: the proximal median nerve, proximal ulnar nerve, distal median nerve, and distal ulnar nerve (objective 3). We implanted four cuffs in each of three cats, and began to follow the cuff impedance and compound action potential (CAP) properties periodically (objective 4c). We also started to design a forelimb reaching task and the hardware required to extract information about contact and slip from chronically recorded nerve activity (objective 4a, 4b).

In the third quarter we built 22 additional nerve cuffs, completing objective 3 for Year One. We implanted four cuffs in each of 5 additional cats, completing a series of 8 cats implanted in the first year. We continued to monitor cuff impedance and compound action potential (CAP) properties periodically (objective 4c) in all 8 cats. The first cat in the series was terminated prematurely at 101 days following device failure. We refined the design of the forelimb reaching task, and started the hardware design (objective 4a,b). We started to obtain the equipment required for in-house histopathological examination of cuffed nerves and contralateral control nerves (objective 5).

In the fourth quarter we continued to monitor the state of the nerves by measuring cuff impedances and compound action potentials (CAP) periodically in seven implanted cats (objective 4c). Several problems relating to long-term implantation of devices have been encountered and are being analyzed. We carried out post-mortem examination of one cat, and based on these findings we are considering some improvements in nerve cuff design (objective 3). Seven Year One cats have been trained with a passive forelimb 2-D manipulator (objective 4a,b), and the 2-D servomotor forelimb reaching task hardware has been re-designed and is being pre-tested for use with the Year Two cats. A histopathological protocol has been developed to investigate the condition of the nerves and implanted devices in the seven remaining Year 1 cats (objective 5). Finally, developments with a sub-contractor have resulted in a change in direction in nerve cuff development (objectives 3, 7).

In the fifth quarter we completed monitoring the Year One series of chronically implanted cats for 6 months (objective 4c). During a final acute surgery, nerve samples were taken from 5 cats for histological examination (objective 5). The average normalized CAP data from 9 nerves followed for 180 days was stable in both amplitude and conduction time. A number of CAP recordings were ended prematurely due cuff wire breakage. We performed a study of the distribution of cutaneous field innervation of the paw from the Ulnar and Median nerves in the cat. In preparation for the Year Two series of implants, we selected 4 candidate muscles in the cat forelimb to retrieve proprioceptive information during movement (objective 6).

III. Summary of Progress in the Sixth Quarter

In the sixth quarter we began implanting the Year Two series of eight chronically implanted cats with nerve cuffs on two of the Median, Ulnar, or Radial nerves and EMG electrodes in four forelimb muscles. We are monitoring CAPs under anaesthesia over the six-month implant period to determine nerve-cuff integrity, and we are also recording voluntary activity in the awake cat during walking on a treadmill and during a reaching and grasping task. A histopathological study of nerve samples from the Year One series of implants has also been initiated.

V. Details of Progress in the Sixth Quarter

A. Year Two implants

In the sixth quarter we carried out four of eight implants planned for the second year, in which we instrumented two of the Ulnar, Median and/or Radial nerves with tripolar cuffs (using the cuff design described in Progress Report #4). The new closing technique that utilizes a stainless steel baton inserted through small Silastic tubes attached to the edges of the cuff is relatively simple to work with in surgery and is very effective, providing a tight cuff closure. This approach also minimizes tangential forces that tended to collapse the cuff tubing when circumferential sutures were used previously to close the cuffs.

In this year's implants we instrumented four muscles in the forelimb with EMG electrodes to monitor voluntary muscle activity during walking, reaching and grasping tasks. These were the four candidate muscles described in detail in Progress Report #5, but with the Palmaris Longus (PalL) in place of the Flexor Digitorum Profundus (FDP) because upon further review, the FDP was considered to be too deep to instrument effectively while the PalL is a large superficial flexor muscle more accessible for instrumentation. The other three implanted muscles were Flexor Carpi Ulnaris (FCU), Extensor Carpi Ulnaris (ECU), and Abductor Pollicis Longus (APL).

In addition to the nerve cuff closing technique, we have implemented a number of other improved surgical procedures in the second series, including a modified backpack anchoring technique and a belly band to restrain backpack movement.

The backpack sutures are made of #5 Mersilene clad with fine Silastic tubing. The effective suture diameter is larger (2.1 mm vs. ~1.0 mm for the suture material alone) and the Silastic tubing does not slide as easily through the tissue. Both factors contribute to reducing the cutting effects associated with backpack movement. In addition, the Silastic tubing prevents foreign materials and fluids from soaking into the suture material and wicking into the body. To date, we have seen no instance of infections around the backpack sutures as were observed in Year One and reported in PR #4.

The animal belly band, made of denim material, attaches to the backpack cover with snaps. It is designed to limit the movement of the backpack and to protect the backpack wires from snagging or breaking, events that occurred a number of times during Year One (discussed in PR #4).

B. Data collection

As in Year One, we are monitoring the status and integrity of implanted nerves and recording cuffs over a minimum six month period by periodically recording CAPs under anaesthesia (objective 4c).

We are also recording voluntary nerve and muscle activity during walking on a treadmill at various velocities and inclines, and reaching and grasping tasks (described in detail in PR #4). The forelimb reaching and grasping task currently involves a passive joystick with a food reward; a computer-controlled device is under construction.

By expanding our range of implants in Year Two to include the Radial nerve and specific forelimb muscles, a more complete analysis of the innervation and voluntary activity in the forelimb will be possible.

C. Histolopathological examination of Year One cats

We have initiated the histopathological examination of nerve samples retrieved from the first series of implants (objective 5). We have nerve samples from five Year One cats in which the nerves were instrumented and monitored for at least six months, and contralateral controls. The aim of the histological study is to determine the extent of nerve damage that may have occurred due to chronic instrumentation of the nerves, and to correlate the nerve condition with CAP data recorded during the implant period. We have also prepared samples available for external investigation.

Personnel turnover has resulted in a new student undertaking the histology studies. The mounting and slicing of nerve samples have been initiated.

V. Plans for Seventh Quarter

In the seventh quarter we intend to:

1. continue histopathological examination of Year One cats (objective 5)
2. continue training Year Two cats on treadmill and forelimb tasks (objective 4a)
3. design and construct cuffs appropriate for smaller proprioceptive nerves (objective 3)
4. complete the Year Two implant series
5. continue monitoring status of Year Two implanted nerves and electrodes (objective 4)
6. complete the construction of hardware for the reaching task (objective 4a,b)
7. record Year Two cats on treadmill and forelimb tasks (objective 4a)